

AMENDMENT & RESPONSE UNDER 37 C.F.R. § 1.116

Serial Number: 09/512,926

Filing Date: February 25, 2000

Title: METHODS TO REDUCE THE SENSITIVITY OF ENDOTHELIALY-COMPROMISED VASCULAR SMOOTH MUSCLE

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Examiner Interview Summary

Applicant's Representative thanks Examiner Jennifer Kim for courtesies extended during the telephonic interviews conducted on April 14, 2003 and April 15, 2003. Claim 1 has been amended as suggested by the Examiner.

Remarks

Reconsideration and withdrawal of the rejections of the claims, in view of the amendments and remarks presented herein, is respectfully requested. Claims 1 and 6 are amended; claims 2-5, 12-22 and 24 are canceled; and claim 25 is newly added. The pending claims are claims 1, 6-11, 23 and 25. The amendments have been made to clarify the claims in order to expedite prosecution of the present application. Therefore, the amendments are not intended to limit the scope of equivalents to which any claim element may be entitled. The amendments to the claims are fully supported by the specification as originally filed.

Support for the amendment to claim 1 is found in the specification at page 13, lines 6-11; in Examples 2-3; and in Figures 1-3.

Claim 6 is amended to correct a typographical error.

Support for new claim 25 is found in claim 1 as originally filed as well as at page 8, line 12; and page 23, lines 17-19, Figures 2-3 and page 23, lines 17-19 of the specification.

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Dkt: 875.039US1**The 35 U.S.C. § 103(a) Rejection**

The Examiner rejected claims 1, 6-11 and 23 under 35 U.S.C. § 103(a) as being unpatentable over Grainger *et al.* According to the Examiner, Grainger *et al.* teach that Applicant's active agent inhibits the activation, including contraction, of smooth muscle cells (page 3 of the Office Action). In particular, the Examiner asserts that the disclosure of "inhibiting contraction" encompasses "normalization," since, according to the Examiner, "inhibition of contraction" would have the same effect as "normalization" of vascular smooth muscle cells (VSMC) (page 3 of the Office Action). As this rejection may be maintained with respect to the pending claims, it is respectfully traversed.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the cited references themselves or in the knowledge generally available to an art worker, to modify the reference or to combine reference teachings so as to arrive at the claimed method. Second, the art must provide a reasonable expectation of success. Finally, the prior art references must teach or suggest all the claim limitations (M.P.E.P. § 2143). The teaching or suggestion to arrive at the claimed method and the reasonable expectation of success must both be found in the prior art, not in Applicant's disclosure (M.P.E.P. § 2143, citing with favor, *In re Vaech*, 20 U.S.P.Q.2d 1438 (Fed. Cir. 1991)).

Claim 1, as amended, is directed to a method to normalize the contractile response of an endothelially-compromised vascular smooth muscle cell in response to a vasoconstrictor agonist in a patient in need of such normalization, comprising administering a pharmaceutically effective amount of a CLC3 blocker, or a pharmaceutically acceptable salt thereof.

Grainger *et al.* disclose a therapeutic method for preventing or treating a cardiovascular or vascular indication characterized by a decreased lumen diameter, wherein a therapeutic agent that elevates the level of TGF-beta is employed (column 2, line 37 to column 3, line 2 and column 10, lines 44-46). Grainger *et al.* disclose that such an agent can inhibit the activity of a VSMC, such as proliferation, contraction, and migration (column 17, lines 41-48), as well as inhibit the "pathological" or "abnormal" activity of VSMC (column 3, lines 17-22 and column 6, lines 15-16), defined by Grainger *et al.* as "division, growth or migration of cells occurring more rapidly

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or to a significantly greater extent than typically occurs in a normally functioning cell of the same type, or in lesions not found in healthy tissues" (column 7, lines 61-65). However, and as conceded by the Examiner at page 4 of the Office Action, there is nothing in Grainger *et al.* that teaches or suggests normalizing the contractile response of an endothelialy-compromised vascular smooth muscle cell to at least one vasoconstrictor agonist. Therefore, Grainger *et al.* do not obviate the pending claims, as amended, and Applicant respectfully requests that the 35 U.S.C. § 103(a) rejection be withdrawn.

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Conclusion

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (612-373-6961) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

FRED S. LAMB,

By his Representatives,

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Date 15 September 2003 By Ann S. Viksnins
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The undersigned hereby certifies that this correspondence is being transmitted by facsimile (FAX NO. 703-308-4556) to: MS AF, Commissioner of Patents, Attn.: Examiner Jennifer Kim, GPO 1617, Washington, D.C. 20231, on this 15th day of September, 2003 (Monday).

Candis B. Buending

Name

Signature

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